

FURTHER STUDIES CONCERNING THE ACTION OF SODIUM CHLORIDE ON THE PITUITARY

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ONE PLATE (SIX FIGURES)

In a previous investigation it was shown that following intravenous administration of hypertonic sodium chloride solutions, distinct morphological changes occur in the pituitary of the rat. These are characterized by the accumulation of large amounts of fluid in the pituitary cleft between the middle and the anterior lobe and by a vacuolization of the anterior lobe basophils which eventually tend to degenerate and to form cystic cavities (Selye, '43). In view of the important role played by the pituitary in connection with water and salt metabolism, it was decided to extend these observations and to determine whether an increase in the dietary salt intake would also elicit detectable changes in hypophyseal structure.

Eighteen male albino rats weighing 60-105 gm. (average 89 gm.) at the beginning of the experiment, were subdivided into two groups. All of them were fed purina dog chow ad lib. but six of them were allowed to drink tap water while the remaining twelve were given only NaCl solution. At the onset of the experiment the NaCl solution was 1.5%, after 2 weeks this was raised to 2% and after 4 more weeks to 2.5%. Rats given very high concentrations of NaCl instead of drinking water usually refuse such solutions, but in our experiment the animals took large amounts, probably because they were allowed to adapt themselves gradually to the salt water. The fluid consumption and output showed great individual varia-

¹ Work performed during the tenure of a National Research Council Studentship.

tions, but while the controls excreted about 1-4 cc. per day on the average, the salt treated rats eliminated 35-50 cc. daily. Four animals in the salt treated group died during the course of the second month of the experiment and all the remaining rats were sacrificed at the end of the second month.

At autopsy the pituitaries of the salt treated rats were distinctly different from those of the controls. The posterior lobe appeared to be edematous and protruded markedly above the surface of the organ. The middle lobe — which is clearly detectable by naked eye inspection as a light ring separating the anterior from the posterior lobe — appeared to be extremely thin and inconspicuous. The anterior lobe, on the other hand, was perhaps even somewhat smaller than normal (figs. 1 and 2). These changes in appearance did not lead to any significant difference in the total weight of the organ which averaged 5.6 mg. in the salt treated and 5.4 mg. in the control animals. It must be remembered, however, that at the end of the experiment the untreated controls were almost twice as large as the salt treated rats whose development was of course inhibited by the excessive NaCl treatment. The average body weight of the controls was 190 gm. (range 180-205 gm.), while that of the NaCl treated animals was 107 gm. (range 95-160 gm.). In view of this difference in body weight the relative weight of the hypophysis was greater in the salt treated than in the control animals.

Upon histological examination it became evident that the most pronounced hypophyseal changes induced by salt treatment occur in the posterior lobe tissue. Even under low magnification this lobe appeared to be diffusely imbued with lightly staining edema fluid and in spots it exhibited a honey-combed appearance due to the presence of numerous vacuoles in the otherwise firmly packed posterior lobe tissue. Upon closer study, especially under high magnification, these small vacuoles were found to result from the presence of numerous pituicytes which were greatly enlarged and in the process of active mitotic proliferation. During mitosis the texture of the cell becomes extremely loose so that the cytoplasm tends to

shrink away from its surroundings and often cells are washed in the course of the staining. In a good many cases, however, the cells engaged in mitosis remained attached to the slide and could readily be identified. The outlines of such cells were exactly the same as those of the empty vacuoles. The presence of many partly shrunken cells whose body was detached from the remaining tissue on one or two points only, confirmed our view that the honey-combing of the posterior lobe is an artifact resulting from the occurrence of numerous cells in mitosis which are lost in the preparation.

The middle lobe appears to be very thin in all the NaCl treated rats and consists only of a few layers of cells. In some cases the cleft between the middle and anterior lobes was greatly distended by fluid just as it was in the previously mentioned acute experiments in which the hypertonic saline solution was administered by the intravenous route. In other cases, however, the cleft was of normal appearance. The borderline between middle and posterior lobe showed certain irregularities in structure which appeared to arise from the degeneration of middle lobe cells in this area.

The anterior lobe revealed no constant pathological change, but in the great majority of the NaCl treated rats the basophils were extremely prominent both in size and in number.

The occurrence of these pituitary changes is of special interest, firstly because mitotic divisions are rarely found in posterior lobe tissue under normal conditions and secondly, because they show that exogenously induced changes in salt and water metabolism may secondarily influence the hypophysis perhaps because they elicit a compensatory defense reaction.

Perusal of the literature revealed no observations comparable to those reported above, but it is perhaps pertinent to mention that according to Hashimoto ('37) diuretics, such as caffeine or diuretin, increase the basophil-count of the anterior lobe of the guinea pig. Similar observations have been made by Goldzieher and Kaldor ('30, '31) and Hashimoto ('37) with novasurol in the same species.

SUMMARY

Experiments performed on albino rats indicate that if concentrated NaCl solutions are given instead of drinking water over a period of several weeks, definite changes appear in the hypophysis. These are characterized by a macroscopically detectable swelling of the organ and the appearance of numerous mitotic figures in the posterior lobe tissue. Simultaneously the middle lobe decreases in size apparently owing to degeneration of many of its cells. Less constantly there appears to be an increase in the fluid content of the hypophyseal cleft and in the number and size of the anterior lobe basophils.

ACKNOWLEDGMENTS

The expenses of this investigation were defrayed through a grant received from the DesBergers-Bismol Laboratories of Montreal, Canada.

LITERATURE CITED

- GOLDZIEHER, M. A., AND J. KALDOR 1930 Studies of the relation of the pituitary to water metabolism. *Proc. Soc. Exp. Biol. a. Med.* vol. 27, p. 799.
——— 1931 Experimentelle Beiträe zur Rolle der Hypophyse in Wasserstoffwechsel. *Z. Exp. Med.*, vol. 76, p. 819.
HASHIMOTO, HARUO 1937 Über die Beziehung der Hypophysenvorderlappenzellen auf den Wasserstoffwechsel. *Mitt. med. Ges. Tokyo*, vol. 51, p. 740.
SELYE, HANS 1943 Experiments concerning the mechanism of pituitary colloid secretion. *Anat. Rec.*, vol. 86, p. 109.

PLATE 1

EXPLANATION OF FIGURES

- 1 Macroscopical view of the hypophysis of a control rat.
- 2 Macroscopical view of the hypophysis of a NaCl treated rat (same magnification as fig. 1). Note prominent and enlarged posterior lobe and atrophic, thin intermediate lobe.
- 3 Section through anterior, middle and posterior lobe of a normal control rat.
- 4 and 5 Section through anterior, middle and posterior lobe of NaCl treated rats (same magnification as fig. 3). Note that the intermediate lobe is atrophic in both cases, but in the pituitary shown in figure 4 the cleft is greatly distended and the posterior lobe is imbued with a light edema fluid while in figure 5 the cleft is normal and the posterior lobe appears "honey-combed" because of the presence of numerous vacuoles and light cells in mitosis.
- 6 High magnification of a cell in mitosis taken from the posterior lobe of the rat shown in figure 5.

